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10/069,280	07/24/2002	Deepak Shukla	MIT-108	7876

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EXAMINER
MAIER, LEIGH C

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 09/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/069,280	Applicant(s) Shukla
	Examiner Leigh Maier	Art Unit 1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-24* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *May 1, 2003* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

Claims 3 and 12-24 have been amended by pre-amendment. Claims 1-24 are pending.

Claim Objections

Claim 17 is objected to under 37 CFR 1.75 as being a duplicate of claim 16. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite a pharmaceutical preparation comprising "a *substantially pure* polysaccharide preparation." (Emphasis added.) The term "substantially pure" is defined at page 6 of the specification as ". . .contain[ing] at least 60% (by dry weight) the polysaccharide of interest, exclusive of the weight of other *intentionally included* compounds." (Emphasis added.)

However, there is no objective standard as to what constitutes being "intentionally included." Thus the claims are rendered vague and indefinite, so that one of ordinary skill would not be apprised of the metes and bounds of the claims.

The claims also recite that the polysaccharide is "enriched for 3-O-sulfated glucosamine residues." At page 5 of the specification, the term "enriched" in a particular polysaccharide structure is defined as "the proportion of the polysaccharide structure in a polysacchairde preparation is statistically significantly greater than the proportion of the polysaccharide structure in naturally-occurring, untreated polysaccharide preparation." By this, it would appear that any polysaccharide comprising a measurable amount of 3-O-sulfated glucosamine would read on this claim. The invention appears to be drawn more particularly to heparan sulfate and derivatives thereof. Even when confining the discussion to this sub-group of polysaccharides, it is well known that these polysaccharides are extremely heterogeneous with regard to sulfation, among other structural differences. While the claims are not really written as product-by-process, (excluding claims 10 and 11) Applicant appears to be reciting the products in terms that compare the level of glucosamine 3-O-sulfation to some "pre-processing" level. However, the products must claimed in terms with objective standards that allows one of ordinary skill to determine the metes and bounds of the claims.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-19 are rejected under 35 U.S.C. 102(b) as being anticipated by CASU et al (WO 98/42754).

CASU discloses heparin/HS and derivatives enriched in 3-O-sulfated glucosamine residues. See page 3, lines 17-21 and examples. It is noted that the compositions are recited "for inhibiting . . . HSV-1 infection." However, the intended use is not a patentable limitation. Further, the claims recite specific binding affinities and oligosaccharide sequences. The reference is silent regarding these features. Nevertheless, the polysaccharide products prepared in the reference do meet the structural requirement of being enriched in 3-O-sulfated glucosamine residues, as required by the independent claims and would necessarily have the properties recited in the dependents.

In the case of claims 10 and 11, these are product-by-process claims. However, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the

prior product was made by a different process. The examiner recognizes that substrate requirements of 3-OST-3 may be such that the product obtained by treating a polysaccharide with this enzyme are objectively distinguishable from products in the art, but the disclosure does not provide a basis to make that deterimination.

Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over ROSENBERG et al (WO 99/22005).

The claims are drawn to a pharmaceutical preparation comprising a polysaccharide enriched in 3-O-sulfated glucosamine residues. Dependents recite HSV-1 gD binding affinities and specific oligosaccharide sequences.

ROSENBERG teaches the treatment of HS with 3-OST enzymes (3-OST-1, 3-OST-2, 3-OST-3, and 3-OST-4) in order to generate novel GAG drugs having utility to treat a variety of disorders. See paragraph bridging pages 50 and 51. The reference specifically exemplifies the use of 3-OST-1. See pages 46-47. Because the reference exemplifies a process resulting in a radioactively labled product, the reference does not specifically *exemplify* a product that would have utility as a pharmaceutical preparation.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a pharmaceutical composition comprising a polysaccharide enriched in 3-O-sulfated glucosamine residues by the enzymatic treatment of HS with 3-OST. The reference specifically suggests the use of several isoforms, including 3-OST-3A and 3-OST-3B, as discussed above. The artisan would be motivated to prepare these processed

polysaccharide products for their art-disclosed utility. It is noted that the compositions are recited "for inhibiting . . . HSV-1 infection." However, the intended use is not a patentable limitation. Further, the claims recite specific binding affinities and oligosaccharide sequences. The reference is silent regarding these features. However, the polysaccharide products prepared in the reference are prepared in the identical manner as that described in the instant disclosure. Therefore, these products would necessarily have identical chemical and physical properties.

Claims 1, 20-22, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over LUKAS et al (US 4,465,666) in view of either:

(1) CASU et al (WO 98/42754) and LYCKE et al (J. Gen. Virol., 1991); **OR**

(2) ROSENBERG et al (WO 99/22005) and LYCKE et al (J. Gen. Virol., 1991).

The invention is as set forth above. Claims 20-22 recite specific types of compositions and components of said compositions. Claim 24 recites a method of inhibiting HSV-1 infection by administering a therapeutically effective amount of the composition described above to a mammal diagnosed with HSV-1 infection.

LUKAS teaches the topical administration of heparin for the treatment of herpes virus (refering to the older name HVH, rather than HSV). See col 1, lines 10-20. The reference further teaches the use of a composition of heparin in a variety of forms, including gels, lotions, creams, etc. comprising skin penetration enhancers, such as ethanol, propylene glycol, etc., with prefered dosages of heparin. See col 4-5.

CASU and ROSENBERG teach the chemically or enzymatically sulfated polysaccharides, as set forth above.

LYCKE teaches that heparin and highly sulfated HS (but not HS with low sulfate content) compete with the cellular receptor for attachment of HSV. See abstract and discussion at page 1135.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer a pharmaceutical preparation comprising a sulfated polysaccharide as taught by either CASU or ROSENBERG for the inhibition of herpes viral infection. LUKAS had taught that sulfated polysaccharides, such as heparin, were useful in treating herpes, and LYCKE had taught that heparin and HS interfered with the binding of the virus to the cell and that the polysaccharide with a higher charge density competes more effectively with the cell receptor. Therefore, one of ordinary skill would reasonably expect success in using these sulfated polysaccharide products to inhibit HSV infection. It would be further obvious to prepare a pharmaceutical composition for this treatment, the composition comprising the sulfated polysaccharide in any appropriate form with the addition of skin penetrating enhancers, as LUKAS had taught that polysaccharide compositions in the recited forms and having the recited additives have utility in the treatment of herpes. It would be within the scope of the practitioner to determine the effective amount of the polysaccharide through routine experimentation.

Claims 1, 20, 23, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over LARM et al (WO 98/05341) in view of either:

(1) CASU et al (WO 98/42754) and LYCKE et al (J. Gen. Virol., 1991); **OR**

(2) ROSENBERG et al (WO 99/22005) and LYCKE et al (J. Gen. Virol., 1991).

The invention is as set forth above. Claim 23 recites a method of inhibiting HSV-1 infection by administering a therapeutically effective amount of the composition described above to a mammal at risk of HSV-1 infection.

LARM teaches the treatment or prevention of infections caused by herpes virus comprising the adminstration of of sulfated polysaccharides such as heparin or HS. See page 2, lines 2-15. The reference further teaches the preparation of compositions in various forms with preferred heparin concentrations. See page 2, lines 19-24 and page 4, lines 1-11.

CASU, ROSENBERG, and LYCKE teach as set forth above.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer a pharmaceutical preparation in an appropriate physical form comprising a sulfated polysaccharide as taught by either CASU or ROSENBERG. LUKAS had taught that sulfated polysaccharides, such as heparin, were useful in treating herpes, and LYCKE had taught that heparin and HS interfered with the binding of the virus to the cell and that the polysaccharide with a higher charge density competes more effectively with the cell receptor. Therefore, one of ordinary skill would reasonably expect success in using these sulfated

polysaccharide products to inhibit HSV infection. It would be within the scope of the practitioner to determine the effective amount of the polysaccharide through routine experimentation.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (703) 308-4525. The examiner can normally be reached on Monday-Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (703) 308-4624, may be contacted. The fax phone number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier
Patent Examiner
September 26, 2003